anti-tumor activity. We hypothesized that partial depletion of CD8 cells might have a similar effect as primary GVHD prophylaxis after allo-PBSCT. We report a series of 25 patients (pts) (median age 47 yrs, 17M/8F) with hematologic malignancies (13 AML, 4 NHL, 3 ALL, 3 MDS, 1 CML, 1 CLL) who underwent PBSCT utilizing HLA matched sibling donors. Pts received cyclophophamide and fractionated TBI (1400 cGy). Stem cells were depleted of CD8+CD3+ T cells with antibody coated high density microparticles (CD8-HDM, Biotransplant, Charlestown, MA). 20/25 were transplanted for advanced disease. GVHD prophylaxis consisted of tacrolimus (0.02mg/kg IVCI daily) alone without methotrexate. Donors were mobilized with filgastrim (10 mcg/kg/d x 5d) prior to stem cell collection. The median number of CD34+ cells infused was 5.9 x 10e6/kg (range, 2.1-22.1 x 10e6/kg), 80% recovery. The number of CD3+CD4+ cells/kg infused was 5.3 x 10e7/kg (range, 1.8-9.0 x 10e7/kg) while the number of CD3+CD8+ cells was 1.9 x 10e5/kg (range, 0.1-5.2 x 10e5/kg), >99% depletion. All patients engrafted. An absolute neutrophil count of 500/l was achieved on Day +10 (range, 9-12). Sustained platelet counts of 20, 000/l were attained on Day +14 (range, 8-42). Chimerism studies revealed 98-100% donor cells in 17/17 pts tested. At 3 months, CD4+ T cells in peripheral blood outnumber CD8 + T cells. The CD4/CD8 ratio was 2.5 (range 0.8-11.9). Most of the CD4+ cells were CD45RO+ while the majority of CD8 cells were CD45RA+. Grades 2-4 acute GVHD occurred in 11/25 patients (44%). Two patients have limited chronic GVHD. With a median follow-up of 270 days (range, 123-376), 20/25 patients (80%) are alive, NED. There have been 4 transplant related deaths (1 pneumonitis, 1 hepatic veno-occlusive disease, 1 Listeria meningitis, 1 GVHD) and 1 relapse. Our results suggest that depletion of CD8+ T cells from mobilized blood with the CD8-HDM device does not hinder hematopoietic recovery after allo-PBSCT. The incidence of acute GVHD was less than that reported in pts receiving a calcineurin inhibitor alone as the sole form of GVHD prophylaxis. Further follow-up is needed to determine the effects of CD8 depletion on rates of chronic GVHD and relapse.

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INFLIXIMAB FOR GVHD THERAPY IN CHILDREN

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Infliximab inhibits TNFα, a major mediator of GVHD pathogenesis. In this retrospective review, we analyzed the use, response and toxicity of infliximab given for 33 episodes of GVHD in 24 children. Ages ranged from 4 mo-18 yrs (median 5y), with 18 subjects <10 yo. Diagnoses included ALL (11), AML (4), SAA (4), and 1 each with ALD, NHL, Fanconi's anemia, Hurler and Omenn's syndrome. Eighteen patients had 25 episodes of aGVHD. Sixteen had steroid refractory aGVHD. In addition, 6/18 subjects were refractory to ATG (3) +/or daclizumab (4). At initiation of infliximab, episodes of aGVHD were grade I-II (11) and grade III-IV (14). Infliximab (10 mg/kg) was administered 1-3x per week. Dosing frequency was increased for 2 patients with protein-losing enteropathy. In aGVHD patients, 110 total doses were given (range 1-58; median 3 doses per flare). Many patients with significant GVHD or symptoms received infliximab combined with other immunosuppressants including: initiation of or an increased dose of MP (3), daclizumab (4), ATG (3), plaquenil (2), MMF (2), thalidomide (1), fludarabine (1) and photopheresis (1). Of evaluable patients, improvement was seen in 15/16 (94%) episodes of skin GVHD [CR 13/16 (81%)] and 11/14 (79%) episodes of GI GVHD [CR 11/14 (79%)]. One of 3 cases of liver GVHD responded. Responses were assessed as the best response within 56 days after starting infliximab. Only 2 of 18 subjects with aGVHD are surviving. Eight patients had 9 episodes of extensive cGVHD. Several patients were treated for an acute flare of cGVHD. The majority of patients were receiving steroids, TAC/CsA and plaquenil. One patient had recently received 2CDA and 2 started daclizumab shortly before infliximab. 426 doses of infliximab (10mg/kg) were given (range 5-162; median 16 doses). Two patients received 157 and 162 doses, resp. Five of 8 patients improved. Only 3 of 8 subjects with cGVHD are surviving with many deaths attributed to cGVHD. Prolonged high-dose infliximab therapy was well tolerated. No infusion related adverse events occurred. Many infectious complications (bacterial, viral, fungal) developed as a result of multi-modality immunosuppression in these high-risk patients. No cases of mycobacterial infections were seen. No increased rate nor predominant type of infection was noted. Infliximab has activity in children with acute and chronic GVHD and warrants prospective analysis.

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MODULATION OF HOST DENDRITIC CELLS BY EXTRACORPOREAL PHOTOPHORESIS IN AN ALLOGENEIC BONE MARROW TRANSPLANT CONDITIONING REGIMEN

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We demonstrated that Extracorporeal Photophoresis (ECP) ameliorates chronic graft-versus-host disease (cGVHD) by decreasing circulating dendritic cell (DC) number and function. To explore whether ECP could prevent GVHD through similar mechanisms, we transplanted 56 high-risk patients with a reduced intensity conditioning regimen of ECP for 2 days, pentostatin (8mg/m2 by continuous infusion over 48 hr), and 600 cGy of TBI. Seven patients (2F, 5M), median age 59 (range 32 to 70), with MDS (n=4), AML (n=1), myelofibrosis (n=1), or NHL (n=1), were studied to determine the effects of ECP on host DC subsets prior to stem cell infusion and DC reconstitution. Flow cytometry used CD11c to identify monocytoid DC1 cells and CD123 to identify plasmacytoid DC2 cells. After the two days of ECP, DC1s decreased a median of 3% (range -39 to +35%), while DC2s decreased a median of 47% (range -100 to +51%). Five patients developed full donor mononuclear cell and DC chimerism by day 100 with no grade 2-4 acute GVHD. In this group, DC1s and DC2s decreased in 2 and 4 patients respectively. Of the 2 patients who failed to engraft, both had decreases in DC1 and one had a decrease in DC2 cells. While our sample size is small, the data suggest that ECP induces similar changes in DC subsets in these patients as in our patients with cGVHD. Since the overall incidence of grade 2-4 aGVHD in 56 patients was 10%, these preliminary data suggest that immunomodulation of host DCs by ECP prior to allogeneic stem cell infusion may play a role in reducing alloreactivity and thereby attenuate the incidence and severity of aGVHD. Further studies will be needed to determine whether these immunomodulatory effects of ECP prior to allogeneic stem cell infusion are correlated with incidence and severity of GVHD in other conditioning regimens.

Age/Sex	Disease	Donor Type	Engraftment	Change in CD11c	Change in CD123	DC Origin @ day100	Acute GVHD
51M	MF	6/6 MRD	DONOR	-39%	-100%	DONOR	1
70M	MDS	6/6 MRD	DONOR	-36%	-90%	DONOR	1
59M	NHL	6/6 MRD	DONOR	29%	-76%	DONOR	0
32F	MDS	6/6 MRD	DONOR	6%	-54%	DONOR	1
59M	MDS	6/6 MRD	DONOR	35%	9%	DONOR	1
40F	AML	6/6 MUD	HOST	-13%	-52%	HOST	NA
61M	MDS	5/6 MRD	HOST	-3%	51%	HOST	NA

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DONOR CD8 T-CELL SUPPORT OF HEMATOPOIETIC PROGENITOR ACTIVITY DURING SYNGENEIC BMT

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Efforts to reduce graft vs. host disease (GVHD) during bone marrow transplantation (BMT) by removing donor T-cells from